REMARKS

I. Claim Status

Claims 1-40 were originally pending, and claims 1-15 and 25-40 were withdrawn from examination prior to the Office Action of July 13, 2010. With this Amendment, Applicants amended claim 16 to incorporate the subject matter of claims 17-19 and 21-22. Accordingly, claims 17-19 and 21-22 were canceled. Claims 20, 23, and 24 were amended to introduce minor changes that make these claims consistent with the foregoing amendments. There is ample support for the above amendments in the original disclosure, for example in at least paragraphs, at FIGs. 1-11, and paragraphs [0014-0015], [0019], [0021-0023], [0038], [0045], [0049-0050], [0054], and [0056].

II. Corrections to Drawings

The Examiner requires corrected drawings because "[t]he lettering is not of proper size, uniform density, and well-defined in Figure(s) 5 and 7-11." Office Action at 2. Previously, in response to the Office Action of July 13, 2009, Applicants submitted substitute sheets of Figures 1, 2A, 2B, 2C, 3A, 3B, 3C, 4A, 4B, 4C, 5, 6A, 6B, 7, 8, 9, 10, and 11 to correct the size of the lettering in Figures 5 and 7-11. Applicants re-submit those replacement drawings with this Amendment because the drawings satisfy the requirements of 37 C.F.R. 1.84(l) and (p)(1)-(5). Specifically, 37 C.F.R. 1.84(p)(1) is directed to: "Reference characters (numerals are preferred), sheet numbers, and view numbers." The size requirements of letters and numerals under 37 C.F.R. 1.84 are set by 37 C.F.R. 1.84(p)(3), which provides "[n]umbers, letters, and reference characters must measure at least .32 cm. (1/8 inch) in height."

Here, the reference and sheet numbers of replacement Figures 5 and 7-11 (*e.g.*, the letters a-d or a-e that refer to the data curves) are at least .32 cm. These Figures do not contain view numbers. Thus, the replacement drawings do not contain any reference characters, sheet numbers, or view numbers that fail to meet the requirements of 37 C.F.R. 1.84(l) and (p)(1)-(5). Accordingly, Applicants respectfully submit that the objection to the drawings should be withdrawn.

III. Rejection under 35 U.S.C. § 112, first paragraph

Claims 16-24 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Office Action at 3. According to the Office, Applicants have claimed a genus of nucleic acid complexes, that, "at the very least . . . comprise two molecules an - oligonucleotide comprising a hairpin-forming sequence capable of forming a stem-loop, and a 'fluorophore-labeled reporter sequence'." *Id.* at 5. The Office then points out that the specification discloses, "[a]s used herein, an oligonucleotide can be a polynucleotide and comprise at least 10, 20, 30, 40, 50, or more nucleotide residues." *Id.* at 5, (citing the specification at 10). Focusing on the phrase "at least 10, 20, 30, 40, 50, or more nucleotide residues," the Office concludes that "[a] review of the disclosure fails to find where applicant has described any oligonucleotide, useful or not, that is 10, 30, 40, 50 or more nucleotides in length." *Id.* at 6. Ultimately, the Office asserts that "applicant has not provided an adequate description of the genus of oligonucleotides that are useful, alone or in complexed formation so that one of skill in the art would be able to identify those that are useful from those that are not useful." *Id.*

In addition, the Office construes the reporter sequence element of the claims "as encompassing not only single-stranded nucleic acids, but also double-stranded nucleic acids, be it dsDNA, dsRNA, or DNA-RNA duplexes, and that the 'hybridization' that is taking place between the oligonucleotide and the reporter sequence can result in the formation of either duplex or triplex strands." *Id.* In short, the Office asserts that there is no description of how the various genera of reporter sequences are to be used in any method that has utility under 35 USC 101." *Id.* at 6. In particular, the Office concludes that sequences disclosed by the specification "present no embodiment of useful RNA molecules, no embodiment of triplex formation, and no embodiment of a useful DNA complex, much less an adequate description of those molecules that are useful such that one of skill in the art would be able to recognize/distinguish useful from non-useful molecules." *Id.* at 6-7. Applicants respectfully disagree.

As an initial matter, Applicants, without acquiescing to the rejection, first point out that their request to enter the above-amendments to the claims. As amended, independent claim 16 recites:

> A nucleic acid complex comprising a capture oligonucleotide hybridized to a fluorophore-labeled oligonucleotide reporter sequence, wherein the capture oligonucleotide comprises at least one guanosine base, and a hairpin-forming sequence capable of forming a stem-loop structure, wherein formation of the stem-loop brings the at least one guanosine base into close proximity to the fluorophore-labeled reporter sequence when the reporter sequence is hybridized to the capture oligonucleotide, thereby quenching fluorescence signals of the fluorophore, and wherein the nucleic acid complex can detect a single-stranded nucleic acid target sequence of any sequence that can form a double-stranded hybrid with a complementary sequence in the stem region of the capture oligonucleotide, wherein the hybridization substantially disrupts the formation of the stem-loop, wherein disruption of the stem-loop produces a detectable increase in fluorescence signals of the fluorophore-labeled reporter sequence.

For the following reasons, Applicants submit that all of the elements of amended claim 16 are adequately described in accordance with the requirements of the first paragraph of 35 U.S.C. § 112.

An adequate written description of the invention may be shown by any sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. Evidence that Applicant was in possession of the claimed invention may include "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *See Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956,964, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

Here, independent claim 16 is directed to a nucleic acid complex that at least comprises: i) a capture oligonucleotide with at least one guanosine base, a sequence capable of forming a stem-loop structure, a sequence in the stem region capable of binding to a complementary single-stranded sequence, and a sequence capable of hybridizing to the reporter oligonucleotide sequence; ii) a reporter oligonucleotide sequence that is labeled with a fluorophore, and that comprises a sequence that can hybridize to the capture oligonucleotide; and iii) an overall structure that allows the at least one guanosine of the capture nucleotide to be in close proximity to the fluorophore of the reporter sequence, such that the fluorophore's signal is quenched, except when

the stem region of the capture oligonucleotide is bound to a complimentary sequence, in which case the formation of a stem loop is disrupted, and the resulting structure prevents the at least one guanosine residue from quenching the fluorescent signal.

The specification provides ample descriptions of each of the characteristics that are listed above. For example, paragraphs [0021-0023] summarize the elements of claim 16. In addition, Figures 1-4, and 6 show detailed schematics of the oligonucleotide structure of the complex. Figures 5 and 7-11 show spectral emission data that collectively demonstrate the direct structure-function relationship between the stem-loop structure and quenching of fluorescence signals. The specification also defines guanosine base quenching as "the reduction in fluorescence emission of a fluorophore when in close proximity to guanosine bases in the sequence of a single or double-stranded nucleic acid." *See* Specification as-filed at ¶ [0048].

All-in-all, the claims relate to a particular arrangement of nucleotide structures, as opposed to a structure that depends on a particular set of sequences. In other words, the size and sequences of the nucleic acid complex of the invention are defined by the extent that the complex is designed to: form a stem-loop structure, quench the reporter sequence fluorophore signaling by placing at least one guanosine base in close proximity to the fluorophore when the stem-loop structure is formed; and not form a stem-loop when a complementary nucleotide sequence hybridizes to the complementary sequence in the stem region, wherein that disruption prevents at least one guanosine base from quenching the signal of the flurophore attached to the reporter sequence. All of the foregoing features of the invention are discussed at length in the specification.

In dealing with biotech patent applications, the Federal Circuit rejected a per se rule for recitation of sequences in *Capon v. Eshhar,* 418 F.3d 1349 (Fed. Cir. 2005), and again in *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006). In *Falkner*, the Federal Circuit also noted that, with respect to written description, examples are not necessary and reduction to practice is not required; such is the case in the present Application. One of skill in the art would have readily recognized that the single-stranded oligonucleotide sequences (targets) that can be detected by the invention are those that can hybridize with a complimentary sequence designed into the capture

oligonucleotide, wherein the hybridization prevents the formation of the stem-loop configuration. In fact, Figures 1-4, and 6 are analogous to detailed blueprints for constructing the claimed nucleic acid complex. Figures 5, and 7-11 in conjunction with the disclosed Examples show the structure-function relationships between the components of the complex, and include exemplified complexes. Moreover, although the claimed complex is novel, the techniques for making the components are well known in the art, and commercially available. Thus, in keeping with *Enzo*, in view of *Falkner*, the specification satisfies the written description requirement because, as discussed above, the specification discloses complete written and graphical depictions of the claimed physical structure of the claimed complex, as well as discusses and exemplifies the relationship between the structural changes that result from having the stem region bound to a complimentary sequence, rather than forming a stem-loop, and the impact of that binding on the fluorescence signaling capacity of the complex. Thus, the specification provides sufficient description to satisfy the written description requirement. Accordingly, Applicants respectfully submit that the rejection should be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

If the Examiner believes a telephone conference could be useful in resolving any outstanding issues, the Examiner is respectfully invited to contact Applicants' undersigned counsel at (703) 776-9703.

Respectfully submitted,

J.A. LINDEMAN & CO. PLLC

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By: /Jeffrey A. Lindeman, Reg. No. 34,658/
Jeffrey A. Lindeman
Reg. No. 34,658